UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,253	06/27/2001	Ignacio Jose Ezquerro Saenz	U013446-9	2595

140 7590 12/30/2004

LADAS & PARRY
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER	
KIM, YUNSOO	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Acti n Summary	Application N .	Applicant(s)	
	09/831,253	EZQUERRO SAENZ ET AL.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

– The MAILING DATE of this communication appears on the cover sheet with th correspondence address –

P riod for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-31* is/are pending in the application.

4a) Of the above claim(s) *26-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

1. The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Yunsoo Kim, Art Unit 1644, Technology 1600.

2. Applicants' Preliminary amendments, filed on 6/11/2001 and 11/20/2001 have been entered. Applicants' amendments filed on 12/16/2002, 5/29/2003, 9/29/2003, 3/25/2004, 6/23/2004 and 10/21/2004 have been entered.

   Claims 1-15 have been canceled.
   Claims 16-31 have been added.
   Claims 16-31 are pending.

3. Applicants' response to Restriction Requirement, filed on 12/16/2002 is acknowledged.

   Applicants' election of Group I with traverse, Claims 16, 17, and 21 drawn to an isolated peptide read upon the elected species SEQ ID NO: 6 is acknowledged.

   Applicant's election with traverse of Group I in the reply filed on 12/16/2002 is acknowledged.

   The traversal is on the grounds that the WO 96/25178 patent does not teach the peptide of claim 1. This is not found persuasive because the prior art as represented by WO 96/25178 discloses TGF-b specific inhibitory agent as a protein or active fragment thereof (i.e. a peptide) (see Detailed Description of the Invention including p7 last paragraph). WO96/25178 teaches using said peptide as an antagonist of TGF-b binding to its receptor, TGF-b type III, also known as betaglycan. The current application recognizes TGF-b1 binds to TGF-b type III receptor (see Detailed Description of the Invention including p.8-14). Therefore, under PCT Rule 13.1 and 13.2, unity of invention does not exist.

   The requirement is still deemed proper and is therefore made FINAL.

Accordingly, as the inventions in claims 16-31 do not relate to a single general inventive concept under PCT Rule 13.1, claims 26-31 are withdrawn from further consideration by the examiner 37 CFR 1.142 (b) as being drawn to a nonelected invention.

Since a prior art revealed no prior art on SEQ ID NO:6, the search has extended to include all of the peptide species. Therefore claims 16-25 are currently being examined.

4. Sequence Compliance: The instant application appears to be in sequence compliance for patent application containing amino acid sequence disclosures.

5. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. PCT/ES99/00375, filed on 5/7/2001.

6. Applicant is reminded of the proper content of the specification and should amend the specification accordingly. It is noted the order in which the specification was disclosed is improper.

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

Or alternatively, Reference to a "Microfiche Appendix": See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.

(e) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(h) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(j) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(k) Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

Applicant is requested to identify the written support for claim 25, particularly the claimed invention of "mimotope".

8. Claim 25 is objected to because of the typographical error. The recitation of "patent" should be corrected appropriately.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 16, 17 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) The phrase " sufficiently similar" recited in claim 16 is ambiguous and unclear and the metes and bounds of the claimed "sufficiently similar" is not defined.

(B) The applicant is reminded that the amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Applicant is invited to consider amending the claims to overcome the rejections

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 16-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection for the following reasons:

The specification as filed does not provide a written description or set forth the metes and bounds of the phrase "amino acid sequence comprising from 9 to 23". The specification does not provide blazemarks nor direction for the above-mentioned range of " 9 to 23 amino acids" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Specification (p.36 cited by applicant) or originally filed claims do not disclose the specific range as recited in claim 16.

Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, Applicant is invited to provide clearly point out the written support for the instant limitations.

13. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated peptide wherein amino acid sequence is selected from the group consisting of SEQ ID NO:3-9, does not reasonably provide enablement for any isolated peptide comprising an amino acid sequence that is sufficiently similar to an amino acid sequence occurring naturally in TGF-beta 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

There is insufficient guidance in the specification as filed as to how the skilled artisan would make and use the amino acid sequence recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for a peptide to inhibit TGF-b binding to TGF-b receptor. Without detailed direction as to which amino acid sequences are essential to the antagonistic activity of TGF-b1 or TGF-b1 receptor peptides, a person of skill in the art would not be able to determine which peptide are antagonistic without undue experimentation.

Furthermore, Applicant has no working examples demonstrating peptides which are sufficiently similar to SEQ ID NOs: 3-9, wherein said peptides maintain antagonistic activity.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

To summarize, reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breath of the claims, it would take undue trials and errors to practice the claimed invention.

14. Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention.

There is insufficient written description encompassing "mimotope which has a longer life in a patient" of isolated peptide because any chemical or physical properties (i.e. chemical structure or specific amino acid changes lead to said function) of mimotope are not set forth in the specification as filed, commensurate in scope with the claimed invention. Claim 25 reads on any amino acid changes of isolated peptides of SEQ ID NOs: 3-9 which have a longer life in a patient but Applicant fails to disclose even a single species within the genus claimed. Therefore, Applicant does not possess of scope of claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Border (WO 96/25178)(see entire document).

Border teaches peptide fragments of betaglycan, a TGF-b III receptor, a receptor recognized to bind TGF-b1, wherein said peptide is disclosed to have antagonistic activity (see Summary of the Invention including p.4, 1st paragraph, Detailed Description of the Invention including p.7-10).

It is noted the claim recites comprising a peptide that is 9-23 amino acids in length. Therefore, the prior art teaching of a fragment reads upon a peptide comprising 9-23 amino acids.

The prior art teachings thus anticipate the instant claimed invention (see entire document including Summary of the Invention and Detailed Description of the Invention).

No claims are allowable. Claims 17-25 are free of art.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yunsoo Kim
Patent Examiner
Technology Center 1600
December 1, 2004

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600
December 1, 2004